## INVOLUTION FORM OF THE TUBERCLE BACILLUS AND THE EFFECT OF SUBCUTANEOUS INJECTIONS OF ORGANIC SUBSTANCES ON INFLAMMATIONS.

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Prof. Robert Koch announced in 1882 the discovery of the cause of Tuberculosis. He claimed that consumption was produced by a *peculiar bacillus of a special shape.* This he described as a rod-shaped micro-organism with rounded ends, either straight or curved, and frequently beaded. This simple form was accepted as a constant character until the summer of 1889, when I first observed, in an artificial culture on an Agar Agar glycerin nidus, a slight inclination to bud in one or more places along the rod, without the production of any particular angle, some relations forming an acute while others formed a right or possibly an obtuse angle. A single bud could only be recognized with a high power objective focused and illuminated with particular nicety. The indications, however, were so often repeated in each field as the slide was moved upon the stage of the microscope that I was sufficiently convinced of the presence of branches to review the life-history of the tube in which they were found and to speculate upon the factors likely to have brought about the evident volution. The result was the production of germs with decided *branches*, some of which were quite as long as the parent rods or stems. This result was published in the *Medical News* of October 19th, 1889. In 1891, Prof. Allen J. Smith observed branched forms of tubercle bacilli in human sputum. Since then Prof. Klein, Herren Fischel, Mafucci et al., have described the branching of this germ. In the summer of 1892 I observed the bacillus in this cycle of life in the liver of the Green Jay of Mexico, *Xanthoura luxosa.* This discovery, coupled with my observations of 1889, and corroborated by the statements of other scientists, must now compel the bacteriological world to recognize a more complex form of the tubercle bacillus than that observed by the great German bacteriologist in 1882. Since the discovery of the branched form of the tubercle germs in 1889, I have been able to continuously reproduce them on artificial mediums. While the young germs seem to be quite simple in form, appearing in straight rods and rods bent upon themselves, those which have arrived at the age of four weeks, particularly in the

presence of an excess of glycerin and in a temperature of 40° C., become branched. The young bacilli, when introduced into the animal tissues, produce tuberculosis, while the older cultures gradually lose their virulence, in all probability owing to their inability to reproduce themselves. This fact indicates that the branched form represents an involution life-cycle of the germ. Notwithstanding the fact, however, that the devitalized, dying or dead bacilli cannot produce consumption, they, with their products, effect a decided increase in tubercular inflammation, which inflammatory process even results in necrosis of the tissues. These phenomena led to investigations proving the correctness of the hypothesis first published in my Monograph on Immunity (Medical News of Oct. 19, 1889) to wit: "It is possible that, by a thorough filtering out of bacilli from tuberculous material, a filtrate might be obtained and attenuated so that by systematic inoculations a change might be produced on living tissues that would enable them to resist virulent tubercle bacilli. In this line of experimentation I proved that the presence of the germs was not necessary to produce the hyper-inflammatory condition of the tuberculous tissue but that it was a *product* of the bacillus that caused the reaction upon the tuberculous animal tissues. This, since called *Tuberculin* and introduced into the human economy for the purpose of curing tuberculosis when introduced into animals suffering with artificially produced tuberculosis, often destroyed the condition called consumption and in many cases appeared to produce immunity to the poison of tuberculosis." The process, however, was not quite so successful in animals which had contracted tuberculosis through one of the natural channels. In these cases, tissues surrounding that which was recognized as tuberculous afterward became infected with consumption. While this was and still is discouraging we have good reason to believe that *Tuberculin* will be permanently established as a remedy for this pathological condition. The toxic albumose causing inflammation of tissues markedly tuberculous, coupled with the fact that it is found in such tissues, led me to inquire whether or not some other constituents of animal tissues, pathological or normal, would produce reaction if introduced in excess into the general circulation. This line of experimentation was begun by first using an albumose of the goat, a comparatively immune animal. This material, however, if at all active as a remedial agent in tuberculosis, is so slow in its effects that I have

heretofore failed to produce any marked changes. When, however, in the course of my investigations I overloaded the animal system with some of its waste products, Dr. William L. Zuill, M. D., D. V. S., who has kindly carried on the clinical work on animals for our Bacteriological Laboratory, reported in the *Times and Register* of Sept. 26th, 1891, a reaction by the Amide group on inflammatory tissues, the animals experimented on being tuberculous. As this group included that which we believe to produce the inflammation of gout, I was led to review my experience with tuberculosis in relation to lithemia. Studying this field with the lithemic and tuberculous habits in view I was soon impressed with the fact that when these diseased conditions were present at the same time in any individual we could claim it to be an exception to the rule.

To determine the special action of the Amide group upon inflamed tissues when introduced into the circulation, a case of Lupus vulgaris was selected and first treated by the subcutaneous introduction of .03240 Gm. of Kreatinin, alternated twice weekly with .130 Gm. of Taurin, Urea and Uric acid. The average temperature during treatment was slightly raised, though not to any very marked degree, under the influence of such small doses. The more recent patches of Lupus, however, became markedly inflamed, being accompanied with a burning sensation. On the third day after the first injection, a marked granulation could be detected around the outer edge by the aid of a strong amplifying pocket glass. This apparently healthy granulation has continued for ten days, in which time the patch has one half of its original area healed. The result shown at this early stage of the experiment is sufficiently encouraging to warrant not only a continuation of the treatment in this case but in other forms of Tuberculosis. The only other subjects upon which these injections have been tried have been cases of pulmonary tuberculosis in a very advanced stage, where there was too much lung-tissue already destroyed to warrant the expectation of a favorable result. The fact that we apparently have an action on the Lupus and no marked result with *small* doses on advanced cases of pulmonary tuberculosis causes me to realize that the line of experimentation must not be confined to tuberculous inflammation but extended to the action of these organic substances on the entire group of inflammatory growths, the effect being produced, possibly, by supplying that in which the pathological tissues are deficient. This line of inquiry, which had

its origin in the Bacteriological Laboratory of the Academy, has opened up a new and wide field of important scientific medical investigation. The main object of this communication, at this time, is to confirm the original discovery of the *branched form* of the tubercle bacillus by recording the observations of the same life-cycle of that micro-organism found in animal tissues. I have, however, ventured to advance theories and results regarding the action of substances far removed from the bacillus, because they were suggested during my studies of the branched form of that organism.